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Phlyctenular Disease of the Eye.

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PHLYCTENULAR DISEASE OF THE EYE

INTRODUCTION

A good deal of interest of late years has been directed to the subject of <sup>h</sup>plycten<sup>n</sup>ular disease of the eye; and there are several reasons to account for this:

In the first place, to take the <sup>b</sup>ophthal<sup>m</sup>ic practice of any large general hospital, the subject is being continually forced home upon one by the frequency with which patient after patient appears with the same complaint. Secondly, one doubts whether the importance of the disease and its grave results are sufficiently appreciated both by the public and the medical profession generally. It is not so much the immediate condition of the phlycten<sup>n</sup>ule that engages our attention; To the casual onserver it may seem trivial enough. It is only in later years when the patient comes complaining of impaired vision that the grave results of the disease are dramatically brought home to us. A slight haziness of the cornea can do so much to damage the eyesight and, now that purulent ophthalmia is being brought more under control, one can safely assert that no pathological condition of the eye is responsible for so much diminution of visual acuity and the cause of so much hardship; Since Koch's discovery of the specific microorganism of tuberculosis and his advocacy of a more rational use of Tuberculin as a diagnostic and Therapeutic agent, increased



(2).

increased impetus has been given to the subject; and it is one of the objects of this thesis to lay stress on the use of Tuberculin in the diagnosis and treatment of <sup>h</sup>plyc<sup>h</sup>le<sup>h</sup>mular disease.



Etiology

In discussing the etiology of phlyctenular disease it may first be noted that in all the cases examined certain predisposing causes appeared common to all. Thus all the cases except two were poor and obviously ill-nourished-- in several cases an examination was made of the housing conditions of the patients. Invariably one found small, over-crowded and ill-lit dwellings with sanitary arrangements of a most primitive character. One could not help noting at the same time the uncleanly and uncared-for appearance of the children. In 12 of the cases measles, scarlet fever or whooping cough had preceded the attack and had left the subjects in a debilitated condition.

As regards age there were none under 3, 2 over 20, one over 15 and the remainder between 3 to 15.

One can unhesitatingly then point to general malnutrition as being a predisposing cause and the school age as being the maximum age incidence.

In endeavouring to ascertain the directly exciting causes a definite conclusion is more difficult to arrive at.

In all the cases of the series of thirty careful examination was made for associated lesions and in no one instance was the phlyctenule the only lesion requiring attention and correction. Most frequently associated was a bad state of the mouth-- in 16 of the cases the teeth were in urgent need of attention. Active caries was present in at least one



tooth and in some cases three or four; and it may here be noted that the affected teeth were on the same side as the phlyctenule. Stomatitis was present in 3 cases.

Next in frequency one noted the presence of hypertrophied tonsils and adenoids; associated was catarrh of the nasal and naso-pharyngeal passages. Thus it was common in these children to see in the region of the nostrils that excoriated condition of the skin indicative of chronic nasal catarrh.

Cervical adenitis was present in 5 cases in 15 cases it was interesting to note that the glands at the posterior border of the sterno-mastoid were palpable as a distinct chain---- W.R. Philip designates these, when present, as a danger-signal of tuberculo-sis.

Impetigo was present in 3 cases and herpes in one case--

The seat of election in the majority of the cases (16 out of 30) was the tempero-malar quadrant.

One was prompted to search for these associated conditions by the suggestion of Harman (1) that in connection with the nerve-supply was to be found the secret of the directly-exciting cause. The supply of the tempero-malar quadrant is afforded by a loop uniting the lachrymal branch of the first division with the malar branch of the second division of the fifth cranial nerve trunk. He considers that an irritative focus elsewhere in the course of the fifth nerve can reflexly disturb the trophic influences of the branches of the same



division and, also, that the two-fold source of nerve control in the seat of election, compared to the single supply of other parts, will favour the more frequent development of phlyctenulae in this than in any other region of the ocular conjunctiva.

The seat of election and the presence of lesions along the course of the fifth nerve in my cases fully bear out Harman's suggestions and that the energetic treatment of these conditions has a bearing in curing and in preventing the recurrence of phlyctenulae will be shown later.

With regard to co-existing ocular conditions, conjunctivitis was definitely present in 6 cases. <sup>(2)</sup> Mayou states that the phlyctenulae are always preceded by conjunctivitis. This could not be satisfactorily established. Blepharitis was present in 4 cases--Errors of refraction requiring correction were present in 8 cases--- 3 hypermetropia -- 2 myopia and the remainder compound astigmatism.

Having taken note of these causes one next directed one's attention to the vexed question, are the subjects of phlyctenulae tubercular?. Most observers in the past contented themselves by dubbing it a nutritional disease and "having" as Fuchs said "its origin in the scrofulous diathesis.

We have now come to regard Scrofula and Tuberculosis as being akin; the kinship has not been positively established but it is well recognised and scrofulous and strumous subjects are



(6)  
regarded, as Continental observers have put it, as  
"candidates for tuberculosis".

(3)  
Stephenson states "while nobody asserts  
that the phlyctenule itself is of tuberculous  
histologic structure, nevertheless it is most  
ordinarily believed that the characteristic lesions  
occur only in those who are subjects of tuberculosis,  
latent or otherwise".

In each case of phlyctenular disease  
examined, endeavour was made to establish the  
presence of tuberculosis. Careful enquiry was first  
made as to tubercular family history--- the patient  
then underwent a thorough examination for tubercular  
lesions in the joints, skin and chest particularly.  
Finally a tuberculin test was employed in all cases.  
There are four such tests. The conjunctival test of  
Calmette was obviously inapplicable-- in out-patient  
practice the hypodermic injection is not practicable  
and Moro's cutaneous test has the reputation of not  
being reliable. On the other hand Von Pirquet's  
cutaneous test is admirably suited to the investigat-  
-ion of ocular maladies--- moreover if the subjects  
of investigation be children the value of the test  
is much enhanced. Von Pirquet himself states that  
the test is of value chiefly in children. He gives  
an analysis of two hundred cases which were ex-  
-amined and which subsequently came to the post-  
-mortem table. His conclusion is that "The positive  
result of the reaction indicates with certainty the  
presence of active or inactive tubercular changes".



The following technique was employed:-,

The skin of the upper arm was washed with soap and water, ether, and, finally with distilled water. Three scarifications were made without drawing blood -- two of these received a drop of Koch's Old Tuberculin. The intermediate one being left as a control. Wolff Eisner divides the local reaction into three grades (a) distinct reaction. (b) strong reaction and (c) very strong reaction, and the results of the diagnostic tests were accordingly recorded. A reaction was considered positive when within forty eight hours the appearance at the site of inoculation showed a papule surrounded by a hyperaemic zone. The reaction of the control is slight and easily differentiated. The behaviour of the reaction with regard to size, duration, intensity etc., seemed to bear no ratio to the intensity of the ocular condition. 16 gave a distinct reaction. 6 a strong reaction and 2 a very strong reaction. The opportunity was taken, when it was possible, to keep the patients in hospital to make a trial of the injection of Koch's Old. T. for the diagnosis of Tuberculosis. Three opportunities offered --- having made sure that the temperature was normal during the previous forty eight hours, 0.00001c.cm. was injected and during the next twenty four hours general, local and focal reactions were noted.



The results are tabulated below:

Cases.	Old T. injected.	General reaction.	Local.	Focal.
P.N. age 12.	0·00001c.cm.	Temp 99 6.	Faint	Faint but de- -cided
G.H. age 15.	0·00001. 0·0001. 0·0009.	Nil. " Temp 101	Nil. " marked	Nil. " very marked
J.B. age 10.	0·00001 0·0001	Nil Temp 102·2	Nil Faint but de- -cided.	Nil. Well mark -ed.

The careful 4 hourly observation of the temperature and the focal reaction render the method unsuitable for hospital practice. Moreover, in the case of G.H. noted above, the <sup>h</sup>plyctenule was partly situated on the cornea and there is every reason to believe that the marked focal reaction produced caused a greater scar formation than would have otherwise resulted--Mac-  
(6)  
-kay gives a warning note in regard to this point.

(2)  
Mayou investigated the tubercular origin of phlyctenulae mainly from the standpoint of the histology of the pathological changes and the bacteriology of the subject. His conclusion is that "The disease, like tuberculosis, is essentially associated with low vitality in the patient and diminished resistance to bacterial invasion; therefore tuberculosis and phlyctenulae are often found together". He does not believe that the one is a cause of the other.



PathologyPathological Anatomy.

The naked eye appearance of phlyctenular conjunctivitis shows a circumscribed nodular eminence, usually situated at the limbus, to which there corresponds a fascicular-shaped injection of the cornea. In the early stages this elevation is conical-- in the process of cure the apex gives way and a minute grey ulcer remains. The ulcer gradually sinks to the level of the conjunctiva and is covered over with epithelium leaving no scar in the majority of cases.

When there is one phlyctenule only the tempero-malar quadrant is the seat of election---but, not infrequently, more than one nodule is present, the whole conjunctiva becomes reddened and the focal character of the inflammation is lost.

The primary occurrence of the phlyctenule on the cornea is not common but it is not unusual to have a spread thence from the limbus. The resulting ulcer is superficial and may leave <sup>no</sup> opacity: in one of the cases treated, however the ulcer spread both widely and deeply in spite of all the measures taken to confine it, and a permanent opacity remained. Occasionally the ulcer is of a serpiginous character healing at one spot and extending at another.

Some authorities state that instead of occurring as foci there may occur a continuous new formation of tissue under the cornea



continuous new formation of tissue under the cornea  
 (7)  
 (pannus) and Herbert believes that phlyctenulae occur  
 on the palpebral conjunctiva.

The nature of the phlyctenule.

The nature and cause of the phlycten-  
 -ule itself have long been a cause of dispute and  
 to this diversity of opinion we may ascribe the  
 succession of names with which the disease has been  
 endowed; most have been founded on what was believed  
 to be the pathological significance of the phlyct-  
 enule -- conjunctivitis eczematosa, herpes con-  
 -junctivae, conjunctivitis scrofulosa or lymphatica  
 are instances.

Phlyctenule means literally a "little  
 bladder" -- the earlier observers believed them to be  
 minute blisters and <sup>(8)</sup> MacKenzie describes the escape  
 of fluid from them. This is not distinctly accu-  
 -rate for if the nodule be fixed in alcohol cut in  
 Paraffine and stained with logwood and eosin it  
 appears to be a solid elevation formed by the  
 accumulation of leucocytes. The projection thins  
 at the apex, the epithelium give way and an ulcer  
 results.

Bacteriology. In studying the bacteriology of the  
 condition, the observer adopted the following pro-  
 -cedure:- Smear preparations and cultures were  
 made from the conjunctival sac. Out of my 10 cases  
 so examined, the nodule being unbroken, the Morax-  
 -Axenfeld bacillus was found in 2 cases and the



Koch-Weeks bacillus in one. The remainder, both smear preparation and cultures, gave negative results. Harman ascribes this freedom from organisms to the profuse lachrymation. 5 cases, in which an ulcer had formed, were similarly examined; numerous organisms were obtained and free growth in the culture medium resulted --- staphylococcus pyogenes aureus was the organism most frequently obtained. Opportunity was lacking for making inoculation experiments; in this connection Fuchs (9) states that inoculation does not lead to tuberculosis nor has the tubercle bacillus been found in the nodule. On two occasions one irrigated the Sac, cocainized the eye and smear preparations and cultures were made from the phlyctenule ruptured for the purpose; staining with carbol fuchsin gave no results. One preparation from each was stained with carbol-fuchsin in the ordinary way but no tubercle was found.

The pathological anatomy and bacteriology therefore gave rather negative results: in view of the tuberculin tests and the results of treatment by tuberculin one adopts the following conclusion:- The phlyctenular nodule is not tubercular pathologically: it occurs in tubercular subjects and develops as nodules do when the skin is rubbed with tuberculin ointment (Moro).



SymptomsSubjectivephotophobia

It is a point for discussion whether true photophobia is present or not: one theory is that the retina becomes sensitive as a reflex result of the effect on the higher centres by the inflamed state of the conjunctiva. But this does not account for its marked presence in some cases and its absence in others. Moreover when atropin was given for corneal phlyctenulae the photophobia was not increased as one would have expected with the dilated pupil. Photophobia is most intense when the site of the phlyctenule is at the limbus or on the cornea, parts with the freest nerve supply. It would be more correct to omit the word photophobia; it is probably simply a blepharo spasm.

Lachrymation. Is as a rule very free, and gives rise to blepharitis, ~~and~~ excoriation and eczema of the lids.

Secretion. As a rule is small in amount, and mucous in nature except when conjunctivitis is associated: as a result sticking of the lids is not common.

On Objective Examination. One's attention is at once drawn by the appearance of one or more small greyish elevations accompanied by a fan-shaped leash of vessels. The remainder of the conjunctiva as a rule remains clear. When the phylctenulae come out in a crop, a not uncommon occurrence, the whole ocular conjunctiva becomes reddened.

When the phlyctenule occurs on the cornea the elevated



nodule and subsequent ulcer are usually superficial. But an appreciable number penetrate the corneal substance and, though the resulting opacity is thin and cloud-like, considerable interference with vision results. Not infrequently nebulae are already present, the legacy of former attacks.

Diagnosis. The focal character of the inflammation and its localization immediately about the cornea are entirely characteristic and peculiar. Fuchs states that nodules occur at the limbus in spring catarrh but these never break down.

#### Treatment.

Immediate Treatment. Immediate treatment of the phlyctenular condition may be said to be satisfactory. The yellow Oxide ointment need not be stronger than Grs 11 to oz 1; what is more important is to ensure that it shall be well rubbed in. When ulceration, pain and photophobia are present atropin should be added. The child should be made to open its eyes in cold water first thing in the morning.

Treatment of Associated Conditions :- One is inclined to believe that insufficient attention is paid to this aspect of treating phlyctenular disease. The rush and overcrowding of these special departments of the large hospitals accounts in some parts for this.

But in the series of cases studied for this thesis every possible cause received careful attention.



received careful attention.

- (1) Suitable glasses were prescribed in the cases of refractive error mentioned.
- (2) Hypertrophied tonsils and adenoids were removed.
- (3) Carious teeth were extracted and in some cases stopped.

Treatment by Tuberculin. The pressing insistent problem, however, is not so much the immediate treatment as the prevention of recurrence and the curing of certain obstinate cases which do not yield to the ordinary treatment. In endeavouring to attain this object the following measures were taken:-

While the conditions associated with phlyctenular disease were in all cases looked for and treated, it was the effect of tuberculin that was studied with most interest.

(10)

Kock is very emphatic about the administration of tuberculin and there can be no doubt that the wave of reaction that set in against its use was the result of employing too strong doses, at too short intervals, while insufficient notice was taken of those small clinical facts, local, focal and general, which constitute a reaction. Treatment by tuberculin moreover, cannot be conducted by rule of thumb. Each case has to be considered separately and on its merits.

The Tuberculins used were:- New Tuberculin T R, mixed types, P.T.O & P.T. (Meister, Lucius & Bruning).



0.00001 C.Cm. might be too large a dose for one case, while 0.0008 C. Cm. might be too small for another. One followed the plan therefore of beginning all cases with 0.00001 C. Cm. T.R. If no elevation of temperature occurred<sup>r</sup> within 24 hours or other evidences of reaction, such as marked reaction at the site of injection (local reaction), reaction at the site of disease (focal reaction), or nausea headache and general malaise (general reaction), the injection was repeated within a week. The dose was varied week by week until 0.00008 C. Cm. was reached. The next series, 0.0001 to 0.0008, was then proceeded with. The scale was gradually ascended until 0.001 C.Cm T.R. was reached.

The administration of P.T.O. then followed, beginning with P.T.O. 0.00001 C.Cm. This is an exceedingly powerful tuberculin and one has to be careful in<sup>its</sup> administration. The interval was increased and the rise in dosage was made more gradual. Any evidence of hypersusceptibility, exhibited by the development of the symptoms above described, was a signal for reducing the dose, omitting it or extending the interval of injection. Haste above all things must be avoided.



Results on the Phlyctenular Disease of Therapeutic Injection.

30 cases studied over a period of 8 months: In 18 cases the ocular disease cleared up completely and there had been no recurrence to date. 60% -- These were regarded as "Cured".

In 10 cases the ocular disease had improved but still required treatment  $33\frac{1}{3}\%$ . In 2 cases the manifestations cleared up under ordinary treatment and, Von Pirquet's test proving doubtful, therapeutic injections were not used. One regrets that the cases have not been under observation for a longer period and that the number of cases has been rather small. But, in spite of these disadvantages, the clinical course of the malady, with its chronicity and its tendency to recurrence, its predilection for the poorly-nourished, its glandular complications, its response to tuberculin diagnostic and therapeutic measures force upon one the association of Tuberculosis and phlyctenular disease and point the way to imperative use of tuberculin as a diagnostic and therapeutic agent of great value.



Summary and Conclusions

The results obtained from the study of cases forming the basis of this thesis justify the following conclusions:-

- (1). That insufficient attention has been paid hitherto to the treatment of defects and lesions so constantly found associated with phlyctenular conjunctivitis.
- (2). That there is an intimate association between phlyctenular disease and tuberculosis.
- (3). That the cutaneous test of Von Pirquet is a reliable method for the detection of Tuberculosis, particularly in children.
- (4). Tuberculin carefully and perseveringly used, is of great value in the treatment and permanent cure of phlyctenular conjunctivitis.



